Claims

1. A crystal of the ZAP-70 kinase comprising the catalytic domain of ZAP-70 kinase with a unit cell dimension of a = 35.77 ± 5 Ångstroms, b = 57.56 ± 5 Ångstroms, c = 80.20 ± 5 Ångstroms ; α = 68.97 ± 5 degrees, β = 89.83 ± 5 degrees, γ = 89.95 ± 5 degrees.

2. A crystal of the ZAP-70 kinase comprising the catalytic domain of ZAP-70 kinase wherein said catalytic domain has a three-dimensional structure comprising the atomic structure coordinates of Table 1.

3. A crystal of claims 1 or 2 wherein the catalytic domain of ZAP-70 kinase comprises the sequence of SEQ ID. No. 2, fragment or a homologue thereof.

4. A crystal of claim 3 wherein the catalytic domain of ZAP-70 kinase comprises at least the ATP-binding site.

5. A crystal of any of claims 1-4 bound to at least one ligand or low molecular weight compound.

6. A computer readable medium comprising data storage material encoded with computer readable data wherein said data comprises the atomic coordinates of Table 1 comprising the catalytic domain of ZAP-70 kinase.

7. A method for making a crystal of a ZAP-70 kinase comprising the steps of:
(i) purification of the full-length ZAP-70 kinase of SEQ ID No.1
(ii) proteolytic domain definition
(iii) expression of the full-length ZAP-70 kinase of SEQ ID No.1 flanked by protease recognition sequences to facilitate proteolytic release of the desired domain of ZAP-70
(iv) expression of the full-length ZAP-70 kinase of step (iii) in a suitable host cell
(v) controlled proteolysis of the desired domain at protease recognition sites
(vi) rapid purification of the desired ZAP-70 domain.

8. A method according to Claim 7 wherein the domain comprises the catalytic domain of ZAP-70 kinase of SEQ ID No.2, fragment or a homologue thereof.

9. A method according to Claim 7 and 8 wherein the catalytic domain of ZAP-70, fragment or homologue thereof is bound to at least one ligand or low molecule weight chemical compound at any step prior to crystallisation.

10. A method of determining the three-dimensional structure of the catalytic domain of ZAP-70 comprising:
(i) crystallisation of ZAP-70 kinase comprising the catalytic domain of ZAP-70 (SEQ ID No.2), fragment or homologue thereof
(ii) utilizing the atomic coordinates of Table 1 in whole or in part to determine the three-dimensional structure of the catalytic domain of ZAP-70, fragment or homologue thereof.

11. A method for determining the three-dimensional structure of a complex comprising the catalytic domain of ZAP-70 kinase (SEQ ID No.2), fragment or homologue thereof bound to at least one ligand comprising:
(i) obtaining x-ray diffraction data for crystals of the complex
(ii) utilizing the atomic coordinates of Table 1 in whole or in part to define the three-dimensional structure of the complex.

12. A method of identifying a ligand or low molecular weight compound that binds to the catalytic domain of ZAP-70 kinase comprising the steps of:
(i) using the three dimensional structure of the catalytic domain of ZAP-70 kinase derived in whole or in part from the set of atomic coordinates in Table 1 to select a potential ligand or low molecular weight compound that binds to the catalytic domain of ZAP-70
(ii) selecting those ligands or low molecular weight compounds that bind to the catalytic domain of ZAP-70.

13. A method of identifying a ligand or low molecular weight compound that binds to the catalytic domain of ZAP-70 kinase according to Claim 11 wherein the catalytic domain of ZAP-70 kinase comprises at least the ATP-binding site of said domain.

14. A method of Claims 12-13 for use in selecting ligands which inhibit the biological activity of ZAP-70 kinase.

15. A method of designing a ligand or low molecular weight compound capable of binding to ZAP-70 catalytic domain comprising:
(i) using the atomic coodinates of Table 1 in whole or in part to determine the three dimensional structure of ZAP-70 catalytic domain
(ii) probing the said catalytic domain of ZAP-70 with a candidate ligands or low molecular weight compounds to determine which bind to the catalytic domain of ZAP-70
(iii) selecting those ligands or low molecular weight compounds which bind to the catalytic domain of ZAP-70
(iv) modifying those ligands or low molecular weight compounds which bind to maximize physical binding properties such as solubility, affinity, specificity or potency.

16. A method according to Claim 15 wherein the candidate ligands or low molecular weight compounds are screened in silico.

17. A method according to Claims 15 –16 for use in designing ligands which inhibit the biological activity of ZAP-70 kinase.

18. A pharmaceutical composition comprising a ligand identified by the methods of Claims 12-14 for use of treatment of diseases and conditions involving T-cell and lymphocyte activation.